The correspondence section is a public forum and, as such, is not peer-reviewed. EHP *is not responsible for the accuracy, currency, or reliability of personal opinion expressed herein; it is the sole responsibility of the authors.* EHP *neither endorses nor disputes their published commentary.*

Good Laboratory Practices and Safety Assessments: Another View

doi:10.1289/ehp.0901755

In a letter responding to an article by Myers et al. (2009), Becker et al. (2009) claimed that industry's Good Laboratory Practices (GLP)-compliant studies are superior to traditional academic peer-review in predicting the risk of toxic agents. I have read almost 30,000 experimental, etiologic, and epidemiologic papers (most in part), and it is evident that industry GLP studies do not report the same risks of a chemical when published in peer-reviewed studies from academia. This may be explained by biases in industry experiments and epidemiology, especially in design, due to the financial interests of industry sponsors—some receiving billions of dollars in revenue per chemical each year. For pharmaceuticals, dozens of published reviews show a strong correlation between industry sponsorship and findings of safety; I know of four such strong correlations in studies of industrial chemical risks (Bekelman et al. 2003; Fagin and Lavelle1999; Swaen and Meijers1988; vom Saal and Hughes 2005).

Becker et al. (2009) relied on a commentary by a former editor at the *Nature* research journals (Jennings 2006) to claim that peer-review gives inferior data compared with GLP studies. Actually, Jennings (2006) wrote about improving, not abandoning, peer review. He presented data showing that the long-term value of scientific papers in neuroscience (judged by experts) correlates with the quality of the journals in which they were published (based on impact factor). That is a cardinal finding because industry supports various journals and their scientific associations, but their GLP studies are rarely published in high-quality journals (again, based on my readings). Evidently, industry's GLP data are not reliable enough to publish, while financial independence of authors and editors, as well as peer review, are markers of good quality data.

Since the widespread experimental testing frauds at Industrial Bio-Test Laboratories (Schneider 1983) and Craven Laboratories (U.S. Environmental Protection Agency 1994), which generated the GLP reforms, industry has issued oceans of GLP-compliant studies for submission to regulatory agencies. Few are submitted for publication, but almost all (in my experience) are submitted to journals that publish many industry-sponsored studies.

Critically, industry and their regulatory agencies took the opportunity proferred by the requirement to comply with GLP to exclude almost all academic high-quality, non-GLP studies from risk assessments of existing chemicals (and the toxicity of new agents are primarily evaluated by the parties who want to sell it). For existing chemicals, I have always found that the effective toxicity doses in regulatory (GLP) studies are higher than those in the peer-reviewed literature, for several end points.

It is important for individuals who value the contributions that science makes to society (reliable data)—or those who are cautious about toxicity of low-dose and cocktail agents that may affect biochemical signals, especially during development—to continue lobbying public agencies to incorporate academia's peer-reviewed studies and to use disclosure of financial interests to give appropriate credence to industry's data in chemical risk assessments. I also call on independent academics to be less competitive and make their methods and data more freely available.

The author works for scientists and nongovernmental organizations, all of which have financial interests that align with public health.

Tony Tweedale
R.I.S.K. Consultancy
(Rebutting Industry Science with Knowledge)
Edinburgh, Scotland
E-mail: tony.tweedale@phonecoop.coop

References

Becker R, Janus E, White R, Kruszewski F, Brackett R. 2009. Good Laboratory Practices and safety assessments [Letter]. Environ Health Perspect 117:A482–A483.

Bekelman JE, Li Y, Gross CP. 2003. Scope and impact of financial conflicts of interest in biomedical research. JAMA 289(4):454–465.

Fagin D, Lavelle M, Center for Public Integrity. 1999. Toxic Deception: How the Chemical Industry Manipulates Science, Bends the Law and Endangers Your Health. 2nd ed. Monroe, ME:Common Courage Press.

Jennings CG. 2006. Quality and value: the true purpose of peer review. Nature; doi:10.1038/nature05032. Available: http://www.nature.com/nature/peerreview/debate/nature05032.html [accessed 19 November 2009].

Myers JP, vom Saal FS, Akingbemi BT, Arizono K, Belcher S, Colborn T, et al. 2009. Why public health agencies cannot depend on Good Laboratory Practices as a criterion for selecting data: the case of bisphenol A. Environ Health Perspect 117:309–315.

Schneider K. 1983. Faking it: the case against Industrial Bio-Test Laboratories. Amicus J (Spring):14–26.

Swaen GM, Meijers JM. 1988. Influence of design characteristics on the outcome of retrospective cohort studies. Br J Ind Med 45(9):624–629.

U.S. Environmental Protection Agency. 1994. Press Advisory: Craven Laboratories, Owner, and 14 Employees Sentenced for Falsifying Pesticide Tests. Washington, DC:U.S. Environmental Protection Agency.

vom Saal FS, Hughes C. 2005. An extensive new literature concerning low-dose effects of bisphenol A shows the need for a new risk assessment. Environ Health Perspect 113:926–933.

Good Laboratory Practices: Becker et al. Respond

doi:10.1289/ehp.0901755R

We appreciate the dialogue stimulated by our letter to the editor (Becker et al. 2009). Our intent was to respond only to Myers et al. (2009) regarding the purpose and function of Good Laboratory Practices (GLP) for weighting reliability of studies. Tyl (2009), in response to Myers et al. (2009), provided extensive point-by-point discussion of the specific studies.

In his letter, Tweedale implies that we argued to *a priori* exclude academic, non-GLP studies from risk assessments. To the contrary, we clearly stated that "[e]ach study, GLP and non-GLP, should be evaluated and weighed in accordance with fundamental scientific principles" (Becker et al. 2009). We fully agree with Tweedale that sources of funding should be disclosed, that researchers should "make their methods and data more freely available," and more industry-supported studies should be published in scientific journals. With respect to bias, Maurissen et al. (2005) and Barrow and Conrad (2006) discussed the spectrum of mechanisms in place to ensure the integrity of industry-sponsored research. Ultimately, all scientific research must stand on its merits. However, it is unscientific to eliminate or devalue any study based solely on the organization that conducted the study, the affiliation of an investigator, or the source of funding. The Society of Toxicology (2008) has stated this principle quite clearly: "[r]esearch should be judged on the basis of scientific merit, without regard for the funding source or where the studies are conducted (e.g., academia, government, or industry)."

Moreover, we did not seek to call into question scientific journal peer review per se, but instead to point out that whereas all study records and data from GLP investigations are available to regulatory agencies, rarely are such details made available as part of a peer-reviewed article published in a scientific journal. The point we wish to emphasize is that typical regulatory safety assessment studies conducted in accordance with GLP *a*) must follow agency test guidelines to assure use of relevant test systems, sufficient and applicable dosing protocols, and adequate dose groups and sizes, and *b*) must evaluate specific end points that regulatory organizations consider validated. Further, such GLP studies submitted to regulatory agencies generally include both a full study report and all raw data. This level of scientific rigor and the extensive data of a GLP study allow a regulatory agency to conduct a comprehensive review and to reach a fully independent conclusion. For these reasons, greater weight and confidence are generally afforded to GLP studies. Now, with the increasingly common practice of journals providing access to

supplemental data, there are expanded opportunities for researchers to disseminate actual study data; this should facilitate independent evaluation by regulatory agencies.

As scientists specializing in regulatory safety evaluations, we have extensive experience in interpreting chemical toxicity studies from government, academia, and private-sector laboratories. In conducting chemical risk assessments, we believe that scientists from all sectors should support the use of objective criteria for determining data quality and study reliability (Schneider et al. 2009) coupled with a structured evaluative framework, such as that of the World Health Organization International Programme on Chemical Safety (Boobis et al. 2006, 2008), to provide a systematic approach for assessing the overall weight of the evidence for observed effects and the postulated mode of action. In this manner, data from laboratory experiments, epidemiological investigations, and cutting-edge mechanistic research from all relevant studies—GLP and non-GLP—and from all investigators, regardless of affiliation or funding source, can be comprehensively reviewed, given appropriate weight, and integrated in a manner that provides a robust, biologically plausible understanding of the potential hazards and risks that exposures to a substance could pose.

This letter has been reviewed in accordance with the peer- and administrative-review policies of the authors' organizations. The views expressed here are those of the authors and do not necessarily reflect the opinions and/or policies of their employers.

The authors are employed by trade associations whose members manufacture and use chemicals.

Richard A. Becker
American Chemistry Council
Arlington, Virginia
E-mail: rick_becker@americanchemistry.com

Erik R. Janus
Crop Life America
Washington, DC

Russell D. White
American Petroleum Institute
Washington, DC

Francis H. Kruszewski
Soap and Detergent Association
Washington, DC

Robert E. Brackett
Grocery Manufacturers Association
Washington, DC

References

Barrow CS, Conrad JW Jr. 2006. Assessing the reliability and credibility of industry science and scientists. Environ Health Perspect 114:153–155.

Becker RA, Erik R. Janus ER, White RD, Kruszewski FH, Brackett RF. 2009. Good Laboratory Practices and safety assessments [Letter]. Environ Health Perspect 117:A482–A483.

Boobis AR, Cohen SM, Dellarco V, McGregor, D, Meek, ME, Vickers C, et al. 2006. IPCS Framework for analyzing the relevance of a cancer mode of action for humans. Crit Rev Toxicol 36:781–792.

Boobis AR, Doe JE, Heinrich-Hirsch B, Meek ME, Munn S, Ruchirawat M, et al. 2008. IPCS framework for analyzing the relevance of a noncancer mode of action for humans. Crit Rev Toxicol 38:87–96.

Maurissen JP, Gilbert SG, Sander M, Beauchamp TL, Johnson S, Schwetz BA, et al. 2005. Workshop proceedings: managing conflict of interest in science. A little consensus and a lot of controversy. Toxicol Sci 87:11–14.

Myers JP, vom Saal FS, Benson T, Akingbemi BT, Arizono K, Belcher S, et al. 2009. Why public health agencies cannot depend on Good Laboratory Practices as a criterion for selecting data: the case of bisphenol A. Environ Health Perspect 117:309–315.

Schneider K, Schwarz M, Burkholder I, Kopp-Schneider A, Edle L, Kinsner-Ovaskainen A, et al. 2009. "ToxRTool," a new tool to assess the reliability of toxicological data. Toxicol Lett 189:138–144.

Society of Toxicology. 2008. Principles for Research Priorities in Toxicology. Available: http://www.toxicology.org/ms/PrinResearch.asp [accessed 12 January 2010].

Tyl RW. 2009. Basic exploratory research versus guideline-compliant studies used for hazard evaluation and risk assessment: bisphenol A as a case study. Environ Health Perspect 117:1644–1651.

ICCVAM: Not Doing Enough

doi:10.1289/ehp.1001969

Anyone interested in the facts about the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and its ineffectiveness, rather than just another ICCVAM/National Toxicology Program (NTP) fluff piece (Birnbaum and Stokes 2010), should read the 2008 front page *Washington Post* exposé of ICCVAM (Gaul 2008) and the PETA report on which the *Post* investigation was based (PETA 2008).

Birnbaum and Stokes' "PR piece" notwithstanding, ICCVAM should be held responsible for failing to abide by its Congressional mandate to support the development and implementation of non-animal testing methods.

Sadly, it appears that the new leadership of the National Institute of Environmental Health Sciences is no more inclined to improve the quality of the science supporting regulatory decision-making than the previous one.

The author is employed by People for the Ethical Treatment of Animals, the largest animal rights organization in the world.

Jessica Sandler
Regulatory Testing Division
People for the Ethical Treatment of Animals
Norfolk, Virginia
Email: JessicaS@peta.org

References

Birnbaum LS, Stokes WS. 2010. Safety testing: moving toward alternative methods [Editorial]. Environ Health Perspect 118:A12– A13.

Gaul GM. 2008. In U.S., Few Alternatives to Testing on Animals. Washington Post, 12 April. Available: http://www.washingtonpost.com/wp-dyn/content/article/2008/04/11/AR2008041103733.html [accessed 19 January 2010].

PETA. 2008. Regulatory Testing: Why Is the U.S. So Far Behind Europe? Available: http://blog.peta.org/archives/ICCVAM%20Report%203-25-08.pdf [accessed 5 April 2010].

ICCVAM: Birnbaum and Stokes Respond

doi:10.1289/ehp.1001969R

Sandler's comments about our editorial concerning the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) (Birnbaum and Stokes 2010) suggest a lack of awareness of the role and significance of the contributions of ICCVAM. The 2008 *Washington Post* article she cites (Gaul 2008) contained many inaccurate statements (a letter correcting the errors was submitted to the *Washington Post,* but it was not published). We appreciate this opportunity to provide accurate factual information about ICCVAM.

ICCVAM is a congressionally mandated committee that does not have laboratories and does not develop test methods or conduct validation studies. Rather, ICCVAM depends on other organizations, including its 15 member agencies, to carry out such activities. The director of the National Institute of Environmental Health Sciences (NIEHS) established ICCVAM in 1997, with the cooperation of 14 other agencies, in order to provide a coordinated interagency process to facilitate the regulatory acceptance of scientifically valid alternative methods. As an interagency forum, ICCVAM also coordinates and promotes related issues, including national and international harmonization, guidance on validation studies, and awareness of accepted alternative methods.

ICCVAM was formally established by legislation in 2000 with signing of the ICCVAM Authorization Act of 2000. This law charges ICCVAM to "review and evaluate new or revised or alternative test methods, … including the coordination of technical reviews of proposed new or revised or alternative test methods …." ICCVAM develops and submits recommendations based on its reviews to the Secretary of Health and Human Services for transmittal to federal agencies. Agencies must review the recommendations and respond to ICCVAM within 180 days. ICCVAM has implemented a transparent and scientifically rigorous evaluation process for test methods that has resulted in national and international regulatory acceptance of all recommended test methods. ICCVAM has contributed to the acceptance of 33 alternative test methods, including 17 based on formal comprehensive evaluations (ICCVAM 2010). Recommendations on an additional 4 methods are pending.

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) administers ICCVAM and provides scientific and operational support for ICCVAM activities. Consistent with the NTP